

### Remarks

Claims 36-54 and 56 are pending and have been rejected. Claims 36, 38 and 43 have been objected to. In response, applicants amend claims 36, 38 and 43, and provide arguments in favor of patentability. A copy of the amended claims, marked up to show changes, is attached. Reconsideration and allowance are requested.

### Claim Objections

On page 2 of the office action, the Examiner has objected to the punctuation used in claims 36, 38 and 43. Applicants have amended these claims as kindly suggested by the Examiner. Further changes of linked punctuation that originally used ";" to match ":" have been altered to "," to comport with accustomed grammatical rules.

Removal of these objections courteously is solicited.

### Claim Rejections Under 35 U.S.C. §103

#### 1. HHP and Merck

Item 3 from page 3 through page 7 of the office action asserts a rejection over alleged obviousness in view of a web page (Hypericum Home Page) or "HHP" and The Merck Manual. This rejection argues (page 3 bottom) that "(HHP) teaches extracts of Hypericum perforatum (St. John's Wort) include hypericin and hyperforin wherein the extracts exhibit anti-inflammatory and antibacterial effects when externally, or topically, applied...." The argument was also presented that the Merck reference evinces a relationship "in the art that aczemas are characterized as superficial inflammations of the skin of varying degrees." (page 4 bottom paragraph).

Prima facie obviousness cannot be built from these two references for several reasons, as follows.

*The HHP Website (www.hypericum.com) Shows That the Copyright Notice was Created no Earlier than 1998*

The "web site" is created by a hypertext language source code that can be seen easily by downloading the actual code that is transmitted over the internet (ie. the information that creates the screen display). A copy of this code is supplied as Appendix A. This code states on line 12 (of the main body) "Created with GDS SmartScript v.4.0 (c) 1998...." Thus, the actual code states that it was "created" with software that was copyrighted in 1998. Assuming that the software writer (or software routine that generated this label) is not lying, the "publication" of this could not have occurred before 1998. This code shows that the "copyright" notice that the Examiner refers to (see the first line of page 4 of the appendix) was created by software having a later copyright of 1998.

Because there is no evidence that the asserted reference is from 1996 and is, in fact, prior art, withdrawal of this rejection is requested.

*Lack of Motivation to Combine Merck with HHP*

On the bottom of page 7 of the office action, the Examiner asserts that "one of ordinary skill (could) determine effective amounts as well as the variety of inflammatory conditions for which known the anti-inflammatory agent is effective, as a matter of routine experimentation. Therefore (a skilled artisan) would have been motivated by HHP to treat inflammatory skin conditions....." However, a showing of motivation requires more than a blanket assertion of motivation, without anything more. The Federal Circuit reviewed this need in the January 18, 2002 appealed case *In re Sang-Su Lee* ( 277 F.3d 1338, 61 USPQ2d 1430). There, the court vacated an Examiner's obviousness finding because "[t]he examiner's conclusory statements ....do not adequately address the issue of motivation to combine" and the "factual question of motivation .....could not be resolved on subjective belief and unknown authority."

Because a specific and objective factual showing for motivation is not presented, the Examiner respectfully is requested to withdraw this rejection for this additional reason.

### *Unexpected Results*

Claim 36 and the other claims dependent thereon recite "a pharmaceutically acceptable carrier." This claim element is not included in the cited references. In fact, St John's Wort Oil is insufficient generally for many claimed uses.

The specification teaches "pharmaceutically acceptable" carriers such as "ointment or cream" as for example stated on page 10, line 37. Particular advantages of this acceptable carrier are also stated on the bottom of page 37. The effects of the ointment and creams (representative pharmaceutically acceptable carriers) "is superior to that of the known St. John's wort oil" as stated on page 11 lines 9 to 10 of the specification. This effect was previously generally unknown and unexpected. Another effect is that "penetration of active compounds" from these particular pharmaceutically acceptable carriers "is superior to that of active compounds from oils." Applicants note in this context that the word "oils" includes plant oils such as plant oil extracts. Such plant oil preparations are NOT included within the group of pharmaceutically acceptable carriers, as is stated here.

Most importantly, applicants discovered to their surprise through investigation that the St. John's wort ointment (i.e. with a pharmaceutically effective carrier) "brings about an inhibition of proliferation (of epidermal cells) . On the other hand, the use of St. John's wort oil results in an increase in proliferation" as seen in the data of Figure 5 from the specification (see page 20 lines 14-18). Clearly, the claimed compositions (not with the plant oil as carrier but with an acceptable carrier) exhibited highly beneficial activity as unexpected results in comparison with the "natural" product promoted and taught by HHP. These unexpected results are strong evidence of unobviousness.

Because unexpected results showed advantageous biological activity of the claimed material compared with the inferior material described by HHP, removal of the obviousness rejection earnestly is solicited for this additional reason.

## 2. Valavichyus and DeCosterd

Valavichyus and DeCosterd do not teach a pharmaceutically effective carrier. St. John's wort oil is not a pharmaceutically effective carrier. Other plant oils apparently are not described properly in this reference or other cited references. Accordingly, a claim element (pharmaceutically effective carrier) is missing for a prima facie case of obviousness. Reconsideration and allowance are requested.

The Examiner argues on page 9, bottom paragraph of the office action, that "Valavichyus specifically teaches oil extracts of St. John's wort is effective for inhibiting sarcoma cells." Even if one assumes that Valavichyus suggests oil extracts generally, such extracts, without more information are not pharmaceutically effective. Furthermore, the science presented in the specification that shows that oil extracts of St. John's wort are undesirable is stronger and more relevant to the claims than is the Valavichyus information. This is because actual skin cells (not a culture of cells many generations removed from the reality of disease processes in humans) were studied directly. That is, when applicants treated real skin of living humans, and then studied cell samples scraped from those subjects, the plant oil (St. John's wort oil) failed miserably and clearly was shown to be a bad carrier. (see page 19 last paragraph through the middle of page 20).

In sum, applicants have obtained data from real in vivo studies that shows that Valavichyus's conclusions are wrong. A skilled artisan following Valavichyus would be led in the wrong direction. To the extent Valavichyus is relevant, it shows teaching away from the claimed invention.

Such evidence of leading away is a further indication of unobviousness.

In contrast, the specification provides ample information regarding the desirable aspects of pharmaceutically effective carriers. As described in the

specification (see Example 11 and associated text) St. John's wort oil is not a pharmaceutically effective carrier. In the context of applicant's specification, which teaches how to use the claimed invention, there is no reason to think that plant oils per se somehow are pharmaceutically acceptable carriers. On the contrary, the oil studied (St. John's wort) was not acceptable and it was found that the active ingredients can be combined with ethanol and cream, as described on page 6 first paragraph, ethanol and greasy ointment base (second paragraph of page 6). Ethanol is particularly useful for the pharmaceutically effective carrier (page 8, second paragraph) and "plant extracts" such as plant oils, if used, are used as ingredients, not carriers per se, as mentioned on page 8 lines 19-22. Crude plant oil extracts generally are not pharmaceutically acceptable. The last paragraph of page 8 through page 9 describes carriers that are acceptable. Plant oil extracts are not in this list.

The cited reference lacks this element that, in contrast, is well described (with examples) in the specification. Accordingly, the reference does not prima facie obviate the claims. Reconsideration and withdrawal of this rejection are requested.

The obviousness rejection presented on pages 10 through 13 of the office action again relies on an idea that "[i]t was also known in the art that plant oils were used as pharmaceutical carriers." Applicants respectfully point out that an acceptable carrier is not a plant oil extract. In fact, the specification provides data showing that a plant oil extract studied was not acceptable and that the plant oil has to be blended with acceptable materials (see the first three full paragraphs on page 9). Any idea obtained from the literature that plant oils are pharmaceutically acceptable for the present claimed invention teaches away from this and indicates unobviousness for this reason. Surprisingly, apparently any plant oil does not work for the claimed invention as the one studied in Example 11 failed. Without any scientific facts supporting the notion that any plant oil is acceptable, the opposite conclusion present in the specification, which is supported by data, must be accepted. Thus, reconsideration and removal of

this last obviousness rejection also is requested because an element of the claim is missing from the cited documents.

In view of the amendments and arguments, reconsideration and allowance of the claims courteously is requested. Should there be any questions, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

March 5, 2003  
Date

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## MARKED-UP COPY OF CLAIMS

36. A method for treating a condition, comprising administering to a subject in need thereof an effective amount of a composition consisting of (a) pharmaceutically acceptable carrier and (b) active agent consisting of (i) hyperforin or (ii) hyperforin and hypericin, wherein said condition is selected from the group consisting of[:]  
cancer[:], an inflammatory skin condition[:], a precancerous condition[:], a geriatric skin condition[:], and a microbial skin infection.

38. The method according to claim 36, wherein said condition is selected from the group consisting of[:]  
exsiccation eczemas[:], hyperkeratotic hand and foot eczemas[:], contact eczemas[:], atopic dermatitis[:], neurodermatitis[:], lichen simplex[:], prurigo simplex[:], lymphomas[:], leukemia[:], melanoma[:], an epithelial pre-cancerous condition[:], tumor metastases[:], and epithelial tumor.

43. The method according to claim 42[:]  
wherein said effective amount is 10 mg hyperforin per ml of the composition.

*Appendix A*

www.hypericum[1]

```
<html>
<head>
<title>Hypericum & Depression</title>
<meta http-equiv="keywords" content="Hypericum, St. Johns Wort, Depression, How To
Survive Depression, Peter McWilliams, Harold Bloomfield, Healing Depression">
<meta http-equiv="description" content="Here you will find, for free, the complete
text of the best-selling book Hypericum (St. Johns wort) and Depression. The
complete text of the book How to Heal Depression, and the latest news and
information on Hypericum. Enjoy.">
<script>
<!--
// Created with GDS SmartScript V.4.0 (C)1998 GD Software V/BNB DK //
http://www.danbbs.dk/~duplex // duplex@mail.danbbs.dk
// ** Copy this script at your own risk ! ;o)
var browser      = '';
var version      = '';
var entrance     = '';
var cond         = '';
// BROWSER?
if (browser == ''){
if (navigator.appName.indexOf('Microsoft') != -1)
browser = 'IE'
else if (navigator.appName.indexOf('Netscape') != -1)
browser = 'Netscape'
else browser = 'NN';
}
// VERSION?
if (version == ''){
version= navigator.appversion;
paren = version.indexOf('(');
whole_version = navigator.appversion.substring(0,paren-1);
version      = parseInt(whole_version);
}
// BROWSER & VERSION
if (browser == 'IE' && version >= 4) entrance = 'yes';
if (browser == 'IE' && version < 4) entrance = 'no';
if (browser == 'Netscape' && version >= 2.02) entrance = 'yes';
if (browser == 'Netscape' && version < 2.02) entrance = 'no';
//-->
if (entrance=='yes'){
name0a = new Image;name0a.src = 'nih.gif';
name0b = new Image;name0b.src = 'nih-on.gif';
name1a = new Image;name1a.src = 'nihr.gif';
name1b = new Image;name1b.src = 'nihr-on.gif';
}

<!-- To avoid MSIE < 4 from crashing
function lighten(imgName) {
if (entrance == 'yes'){
imgOn = eval(imgName + 'b.src');
document[imgName].src = imgOn;}
}
function darken(imgName) {
if (entrance == 'yes'){
imgOff = eval(imgName + 'a.src');
document[imgName].src = imgOff;}
}
//-->
</script>
</head>
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Page 2

www.hypericum[1]

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<a href="articles/times.htm">L.A. Times front-page story on St. John's wort</a>
<p>
<a href="articles/Testingpills.htm">L.A. Times test results of St. John's wort</a>
<p>
<a href="articles/whatshap.htm">So what Happened with the LA Times Testing?</a>
<p>
<a href="goodnews.htm">Good news about St. John's wort and the treatment of
alcoholism</a>
<p>
<a
href="http://www.amazon.com/exec/obidos/external-search/?keyword=Hypericum+St+Johns+
wort&tag=petermcwilliamsh">To search for other books on Hypericum (St. John's wort),
click here</a>
<p>
<a
href="http://www.amazon.com/exec/obidos/external-search/?keyword=depression&tag=pete
rmcwilliamsh">To search for other books on depression, click here</a>
<p>
<a href="http://www.realsjw.com">Acquire research-grade SJW from McWilliams
estate</a>
<p>
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www.hypericum[1]

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<small>Copyright &copy; 1996 Harold H. Bloomfield, M.D. and <!a
href=mailto:peter@mcwilliams.com> Peter McWilliams</a>
  <p>
  <!a href="http://mcwilliams.com/credits.htm"><!Site credits></a></small>
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